Résumé

L'avortement thérapeutique dans une ville canadienne

Dans une ville canadienne de 200,000 habitants, il a été procédé à 119 avortements thérapeutiques au cours d'une période s'étendant de 1962 à 1968. Les raisons invoquées pour procéder à ces avortements étaient multiples, mais parmi elles figurait souvent la dépression. L'absence de collaboration de la part des proches a joué un rôle pour emporter la décision. En fait, cinq psychiatres seulement sont intervenus dans les 82 cas envoyés en consultation psychiatrique. Les avortements pratiqués pour des raisons plus classiques, la rubéole par exemple, ont diminué de 1967 à 1968. Mais, à partir de 1967, on notait une augmentation globale du nombre d'avortements. Durant les deux dernières années de la présente étude statistique (1967-68), on a noté une plus forte proportion de filles célibataires, très jeunes, qui n'avaient jamais été enceintes et qui, du reste, finirent par obtenir un avortement. Un nombre plus élevé furent stérilisées.

En 1969, 166 avortements ont été pratiqués. Un chiffre comparable (179) a été fourni par une autre ville canadienne, tandis que dans une autre ville, on comptait 291 cas et, dans deux autres, 106 et 63 respectivement. Pour l'ensemble des 27 autres localités ayant répondu au questionnaire, on n'en comptait que 186.

Congenital malformations: preliminary report of an investigation of reduction deformities of the limbs, triggered by a pilot surveillance system

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Summary: A brief account is given of a pilot study–surveillance system of congenital anomalies. The steps taken to investigate a suspected increase in the numbers of infants born with reduction deformities of the limbs are described. Information is presented concerning 35 infants with reduction deformities of the limbs and other deformities born in four provinces during 1969. The importance of accurate reporting of all congenital malformations on vital statistics documents and on hospital records is emphasized. It is concluded that: (1) The pilot study-surveillance system is capable of demonstrating changes in incidences of anomalies and of initiating follow-up studies within a reasonable length of time; and (2) The information collected on these 35 patients, while not sufficient to establish the etiology of the anomalies, does suggest that no currently recognized factor has been identified for the majority of these cases and that there is a great need for further detailed investigation of possible etiological factors.

In response to a demonstrated need for more information on congenital malformations, the Department of National Health and Welfare established the Expert Committee on the Occurrence of Congenital Anomalies. Acting upon the recommendations of this committee, a pilot study of a surveillance system of congenital anomalies was started in 1966.

With the co-operation of New Brunswick, Manitoba, Alberta and British Columbia, information has been collected on the incidence of congenital anomalies in infants born in these provinces since that time. The system covers some 93,000 births a year or about one-quarter of the total number of Canadian births.

The purpose of this report is to draw attention to this pilot study and to the continuing problem of congenital anomalies by reporting preliminary results from an investigation of infants born with reduction deformities of the limbs.

At the end of June 1969, in reporting an additional two infants with reduction deformities of the limbs born that month, Dr. C. S. Dafoe of the Alberta Registry for Handicapped Children and Adults expressed concern about the number of these cases reported to the registry since the start of the year. The incidence of limb deformities was under scrutiny here since the receipt of an unconfirmed report from the United States of infants with these malformations being born of mothers taking hallucinogenic drugs.

By the end of June 1969 the Pilot Study–Surveillance System had received reports from the four provinces of 23 infants with reduc-

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tion deformities of the limbs with absence of tissue born in the first six months of that year. Such deformities may be defined as an absence of bone or cartilage and/or absence of digit, hand, foot, forearm, leg, arm or thigh. The number of infants born with absent hands, feet, legs or arms, and notified to the Pilot Study–Surveillance System numbered 13 in 1966, eight in 1967 and 12 in 1968. Of the abovementioned 23 infants born in the first half of 1969, 12 had reduction deformities of the limbs of comparable severity. Since at this time (July 1969) there did not appear to be a change in incidence of other types of malformations, it was decided to launch a preliminary investigation rather than wait to see if the upward trend in incidence of reduction deformities of limbs would continue.

Methods

The Pilot Study–Surveillance System operates in the following way:

In each of the four participating provinces the Physician's Notice of Live Birth or Stillbirth forms and the medical sections of stillbirth and death registration forms are screened for any entry describing a congenital anomaly. In the case of death registration forms, only infants aged less than one year are included. A copy or an extract of the form, containing the written description of the anomaly, together with identifying data, is forwarded by provincial authorities to the Division of Child and Maternal Health, Department of National Health and Welfare at approximately weekly intervals.

The information is coded using the eighth revision of the International Classification of Diseases, Adapted,[1] entered on punch cards and evaluated at one- to two-monthly intervals. Tables of selected anomalies are prepared and sent to the participating provinces at the time of evaluation. A full description of the Pilot Study–Surveillance System together with the statistics accumulated for three years of operation will be published separately.

The cases involved in the follow-up were all notified to the Pilot Study–Surveillance System. Since this was the first episode to be investigated, no standard procedure had been defined.

The following steps were taken:

1. The departments concerned in each province were asked to verify the diagnosis and obtain information about the pregnancy for each case. Three different methods of follow-up were used by the four provinces: (a) Questionnaires were sent to local medical officers of health for completion. (b) Questionnaires were sent to the physician who delivered the baby and to the local public health nurse for completion. (c) Permission was obtained from the physician in charge of the patient for a physician in the provincial department of health to question the parents directly.

As information became available it was sent to the Division of Child and Maternal Health, Department of National Health and Welfare.

2. A careful search for cases which might have been missed in the records of the Pilot Study–Surveillance System was carried out.

3. Hospital insurance admission-separation forms in three of the four participating provinces were screened.

4. A field visit was paid to the city with the largest number of cases. This led to a review of the hospital records of all affected infants born there and discussion with provincial authorities about more detailed studies.

5. Members of the provincial departments of health in the remaining six provinces were advised of this trend by telephone and later by letter, and were asked about the possibility of obtaining information concerning the incidence of infants born in 1969 with reduction deformities of the limbs.

6. Colleagues in other countries were contacted informally to enquire if they had noted any unusual increase in limb malformations.

Results

The data presented were obtained from notifications to the Pilot Study–Surveillance System, follow-up reports from the provinces and a review of hospital records.

TABLE I

Reduction deformities of limbs by province, year and month of birth for 6-month periods (January to June)*

	1966		1967		1968		1969	
	Cases	*Rate†*	*Cases*	*Rate†*	*Cases*	*Rate†*	*Cases*	*Rate†*
New Brunswick	3	46.6	4	63.6	2	34.1	3	52.1
Manitoba	3	32.2	3	34.7	6	69.0	3	32.1
Alberta	7	45.3	3	19.5	6	39.6	11	71.1
British Columbia	4	24.6	9	53.9	5	30.0	8	44.8
Total	17	35.8	19	40.4	19	41.0	25	51.6

*Including reports received up to July 1969.

†Per 100,000 live births.

Note: Rates are based on the numbers of live births as reported in Dominion Bureau of Statistics annual and monthly "Vital Statistics".

In these "rates" the denominators, live births, do not include stillbirths and infant deaths, which may be represented in the "cases".

TABLE II

Revised* estimate of frequency of reduction deformities of limbs by province, year and month of birth for 6-month periods (January to June)

	1966		1967		1968		1969	
	Cases	*Rate†*	*Cases*	*Rate†*	*Cases*	*Rate†*	*Cases*	*Rate†*
New Brunswick	3	46.6	4	63.6	2	34.1	3	52.1
Manitoba	3	32.2	3	34.7	7	80.5	3	32.1
Alberta	7	45.3	3	19.5	5	33.0	15	96.9
British Columbia	4	24.6	9	53.9	5	30.0	6	33.6
Total	17	35.8	19	40.4	19	41.0	27	55.7

*December 8, 1969.

†Per 100,000 live births.

See also Notes to Table I.

TABLE III
Infants with reduction deformities of limbs grouped by site and combinations of anomalies

Description	*No. of cases*
Upper limb only	12
Lower limb only	3
Upper and lower limb only	2
Reduction and other limb malformations only	4
Limb and other malformations	14
Reduction deformities of limbs with absence of tissue.....Total	35

Review of all cases with limb malformations reported to the Pilot Study–Surveillance System for the previous three years led to the discovery of additional infants with reduction deformities, mostly absence of digits. Two new cases were discovered for 1968 and two for 1969 from the hospital insurance admission and separation records available from three of the four provinces. These four cases are not included in this report, since they were not notified through the surveillance system.

The situation one month after the investigation started is shown in Table I. Selection of the first six months of the year was an arbitrary one and reflected merely the time at which the investigation was started. Infants with reduction deformities born after June have also been included in the follow-up.

At the time of writing (December 1969) we have been notified of 37 infants born between January and September, 1969, with reduction deformities of the limbs associated with absence of tissue. On follow-up two of these infants were shown not to have absence of tissue, leaving 35 cases as the subjects of this report, although information is not complete for all cases. The distribution by province of the cases born January to June 1969 is shown in Table II.*

Deformities

The written descriptions of anomalies of the limbs obtained from the previously mentioned source documents have not always been adequate for diagnosis. In particular, the use of the term phocomelia has been inaccurate. Although information from follow-up is sufficient to establish that 35 infants have reduction deformities of the limbs with absence of tissue, radiographs and/or photographs or drawings are not available for enough cases to allow exact classification as suggested by O'Rahilly[2] and Birch-Jensen.[3] The severity of the limb deformities varies from the absence of a single digit (one case) to complete absence of all four limbs (one case). Tables III and IV provide information about the severity of the limb reductions.

TABLE IV
Infants with reduction deformities of limbs grouped by most severe limb anomaly reported

Deformity	*No.*
Absence of arm* or thigh*	5
Absence of forearm* or leg*	3
Absence of hand or foot	4
Absence, of all or part of radius, ulna, femur, fibula	9
Absence of digits	14
Total	35

*As used in nomina anatomica.

As may be seen from Table III, 18 infants had multiple malformations. Anomalies reported have been grouped by system, and the results are shown in Table V. Since one infant might have anomalies in different systems, and in fact more than one anomaly in one system, the totals reflect only the number of times a system anomaly has been reported in the 18 cases.

Information about the laterality of the reduction deformities is available on 33 infants and is presented in Table VI. One infant had chondrodystrophia calcificans congenita, a recessively inherited type of dwarfism.

TABLE V
Systems affected by anomalies in 18 infants with multiple malformations

Site of anomaly	*No.**
Limbs (not reduction type deformity)	10
Genitourinary system†	8
Gastrointestinal system**	8
Central nervous system	8
Cardiovascular system	6
Musculoskeletal (excluding limbs)	5
Special senses	2

*Number of infants with malformations reported in the specified system.
†Includes two cases with rectovaginal fistula.
**Includes one case with tracheoesophageal fistula.

Deaths

There was one stillborn infant and 10 others died. As might be expected, all the deaths occurred in the 14 infants with multiple congenital malformations involving sites other than the limbs.

Sex distribution

There were 17 male and 17 female infants and one of uncertain sex.

Birth weight and gestation

Information about birth weight and gestation is available for 28 of the infants. Excluding infants with absence of arms and/or legs, nine of the 23 remaining patients were of low birth weight. Using the relation between birth weight and gestational age described by Pusey and Haworth,[4] three infants were more than two standard deviations

TABLE VI
Reduction deformities of limbs by side involved in 30 infants*

Site	*Right*	*Left*	*Both*	*Total*
Upper limb only	9	6	3	18
Lower limb only	2	4	2	8
Upper and lower limbs	—	—	4	4
Total	11	10	9	30

*Not included: one case with bilateral upper and right lower; one case with right upper and right lower; and one case with left upper and right lower.

*Approximate tests indicate that in Table I there are no statistically significant differences in comparisons among provinces for the same year or among years for the same province, but in Table II the Alberta incidence in 1969 is significantly higher (5% level).

TABLE VII
Distribution of mothers by age and year

Age in years	Mothers of affected infants		All mothers—New Brunswick, Manitoba, Alberta, British Columbia			
	1969		1968		1967	
	No.	%	No.*	%	No.*	%
0–14	0	—	<.1	<1	<.1	<1
15–19	5	17.9	13.1	14.0	13.0	13.8
20–24	7	25.0	33.6	35.9	32.9	35.0
25–29	8	28.6	25.2	26.9	24.3	25.8
30–34	5	17.9	12.9	13.7	13.5	14.4
35–39	1	3.6	6.6	7.0	7.6	8.1
40–44	2	7.1	2.1	2.2	2.4	2.6
45–49	0	—	.2	<1	.2	<1
50+ or not reported	0	—	<.1	<1	<.1	<1
Total	28	100.0	93.8	100.0	94.1	100.0

*In thousands.

less than the mean birth weight for the stated gestational age, and six were below the 10th percentile. Of these nine infants, four died and one was stillborn.

Family history of congenital anomalies

Information was reported on this topic for 26 cases. Ten cases had family histories positive for some kind of malformation, of which seven recorded a limb anomaly not of a reduction type. Two relatives had clubfoot alone, one had clubfoot and cleft lip, and one had polydactyly; the three remaining anomalies were poorly documented. It is unfortunate that information on consanguinity is known for only two cases (both negative), and on ethnic origin in five cases. These enquiries included any known relative.

Age of mothers and pregnancy order

Information for 28 of the 35 mothers in this series is compared in Tables VII and VIII with similar data for all mothers in New Brunswick, Manitoba, Alberta and British Columbia, 1967 and 1968. There is no significant difference between the two groups.

Conception and birth

Fig. 1 shows the month of birth for the 35 infants with reduction deformities. In 28 cases the length of the gestation was reported, and the month of conception has been derived from this information and shown in Fig. 2.

Drugs

From Table IX it may be seen that 78 drug uses were reported by the 29 mothers from whom information was obtained. A total of 38 drug uses were reported by 21 mothers during the first trimester of pregnancy (first 12 weeks). This included six mothers who took vitamins and iron only. It seems unlikely that reliable information was obtained about the use of hallucinogens.

Complications and illness during pregnancy

Reports from 29 patients gave specific information about complications of pregnancy or illnesses which occurred during this period; this is summarized in Table X. Thirteen mothers reported illnesses or complications during the first trimester and one patient reported an automobile accident. Seven mothers reported no illnesses or complications throughout pregnancy.

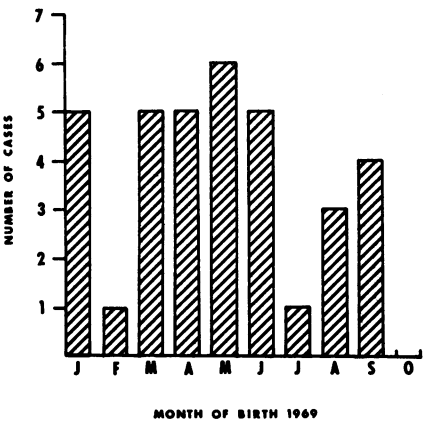

FIG. 1—Month of birth, 35 infants with reduction deformities of limbs.

Other information

Seven of 27 mothers reported radiographs taken during pregnancy, four of which were taken in the last trimester and were of the abdomen or pelvis. One mother reported a chest radiograph early in pregnancy, one an x-ray of her face early in pregnancy following a car accident, and a third a chest radiograph at an unstated time. Eight mothers were reported as smokers and eight as non-smokers. Dietary information was recorded in a minority of cases; the intake of low-calorie drinks was reported as nil in three cases and one to two bottles a week in one case. Chromosomal studies were carried out in three infants and were normal. Of 16 mothers from whom family planning histories were obtained, eight had used oral contraceptives at some time.

While information on reduction deformities of the limbs has been received from three of the six non-participating provinces, the different methods used in collection of the data do not allow any conclusions to be drawn at present.

Information from other countries is still being received, and no comment is possible at this time.

Discussion

A surveillance system designed to give early warning of changes in incidence rates of congenital anomalies must cope with the inevitable delay between the exposure of the embryo to an adverse effect and the diagnosis of the congenital malformation. It has been suggested recently by Shepard and Hollingsworth[5] and by Miller[6] that this delay can be partially circumvented by monitoring abortuses for

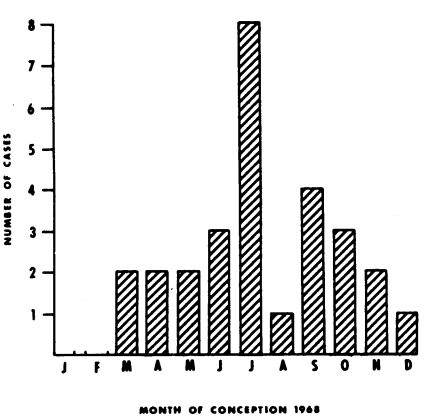

FIG. 2—Month of conception, 28 infants with reduction deformities of limbs.

anomalies. To be effective, the surveillance system must keep to a minimum the time lag between the notification of the congenital malformation and its statistical evaluation. Inevitably this means that the data examined will be of a preliminary nature, since detailed and accurate reporting and speed of reporting appear to be inversely related. In deciding to follow up infants with reduction deformities of the limbs who were born in 1969, on the basis of evidence available in July 1969, attention had to be paid to the fact that we were comparing the preliminary figures for these months with the final figures for the first six months of the previous three years. In fact, comparison of Table II, which gives the current picture for the first six months of the year, with Table I shows changes in two of the provinces.

The eight additional infants included in the follow-up studies were born in July, August and September. While reports are not complete, this number is not higher than has been reported for previous years.

Changes in reporting techniques may also be responsible for fluctuation in rates; Table XI is presented to show rates for various anomalies for six-month periods. Some of these anomalies are among those believed to be associated with exogenous factors. Since there has been no marked upward trend in other anomalies, an examination of these figures does not suggest a sudden change in reporting techniques even if it does not exclude it. It is believed that ascertainment is fairly complete for the reduction deformities of the limb for 1968 and 1969, and a close watch will be maintained over trends for 1970.

It is important to know that the anatomical lesions described are similar over this three-and-a-half year period. With the International Classification of Diseases, Adapted, a considerable number of conditions may still exist within the same four-digit code category. In the Pilot Study–Surveillance System the accessibility of the written description of the anomaly facilitates comparison once the cases have been identified by code numbers, allowing the matching of similar anomalies over the years.

About half the cases had other malformations in addition to the reduction deformity of the limbs. In 14 of the 35 infants absence of digits was the most severe reduction deformity, although some of these had severe malformations of other systems. The commonest associated anomaly was another type of malformation of the limb; next most common were anomalies of the gastrointestinal tract and the genitourinary system. It is interesting that Leck *et al.*[7] recently described an increase in reduction deformities of the digits in infants born to mothers exposed to epidemic influenza in the U.S.A. in 1963. In another paper Leck[8] describes increases in cleft lip, esophageal atresia, imperforate anus and exomphalos following influenza epidemics in Great Britain. In this series (Table X) three mothers reported four attacks of influenza during the first 12 weeks of pregnancy; deformities in their infants were multiple, and included cleft palate in one and imperforate anus and tracheo-esophageal fistula in another.

One of the features of thalidomide-affected infants was the high percentage with bilateral lesions. Table VI shows that this is by no means so in our cases, and where there is unilateral involvement it is as often on the right as on the left side.

Ten mothers out of 26 who gave information about the family history stated that there had been previous experience of congenital anomalies in the family. However,

TABLE IX
Drug use reported during pregnancy in 29 mothers

Name or type of drug	*No. of reported uses and stage of pregnancy at time of use*					
	1st trimester	*2nd trimester*	*3rd trimester*	*all 3 trimesters*	*not stated*	*Total*
Iron		5	1	5	3	14
Vitamins		4	2	6	4	16
Diuretics	—	—	6	—	—	6
Salicylates	4	—	1	—	—	5
Barbiturates	2		1	1	—	4
Bendectin	3	—	—	—	—	3
Other antinauseants	3	—	—	—	1	4
Sulfonamides	—	1	1	—	1	3
Penicillin	1	1	—	—	—	2
Dilantin				2	—	2
Tranquillizers	1	—	1	—	—	2
Laxatives	1	—	1	—	—	2
Anthelmintics	2	—	—	—	—	2
Antacids	1			1	—	2
Cannabis	1	—	—	—	—	1
Others	4	2	1	—	3	10
Total	23	13	15	15	12	78

TABLE VIII
Distribution of mothers by pregnancy order and year

Pregnancy order	*Mothers of affected infants*		*All mothers—New Brunswick, Manitoba, Alberta, British Columbia*			
	1969		*1968*		*1967*	
	No.	*%*	*No.**	*%*	*No.**	*%*
1	11	39.3	33.8	36.1	32.1	34.1
2	6	21.4	24.9	26.6	24.0	25.5
3	3	10.7	14.5	15.5	14.8	15.7
4	4	14.3	8.4	8.9	9.1	9.7
5	2	7.1	4.5	4.8	5.2	5.5
6	0	—	2.7	2.8	3.0	3.2
7 and over	1	3.6	5.0	5.3	5.9	6.2
Not stated	1	3.6	<.1	<1	<.1	<1
Total	28	100.0	93.8	100.0	94.1	100.0

*In thousands

no conclusions can be drawn from this except that, since the malformations in the relatives did not resemble those in the patients, it seems unlikely that a major mutant gene is involved in many cases, and even more unlikely that the presumptive increase in limb-reduction deformities has a genetic basis.

In view of the known inaccuracies in calculating the length of gestation, more particularly in abnormal infants, it would be unwise, without further data, to attribute much significance to the large number of conceptions which were calculated to have occurred in July, especially since so few were recorded in August.

In the National Institutes of Health collaborative perinatal research project, data on drug intake have been gathered for some 56,000 pregnancies, but it is proving difficult to draw conclusions from this information.[9] Recently Bendectin,[10] Stelazine,[11] Dilantin[12] and salicylates[13] have all been mentioned in association with the birth of infants with congenital malformations. Although three mothers of infants in our series reported taking Bendectin and one Stelazine, a small survey done in maternity and general hospitals in an urban area[14] showed that of 66 mothers who were questioned soon after delivery, 12 said they had taken antinauseants during their pregnancies, and while the particular drug was not known in every case, at least five and probably six of these mothers had taken Bendectin and three or four had taken Gravol. A personal enquiry directed to obstetricians in another city suggested that a high proportion of all mothers with nausea might be exposed to these drugs. The congenital anomalies of the infant in this series whose mother had taken Stelazine were not similar to those reported.[11] Dilantin was used during the first trimester by two mothers; anomalies in their infants, again, were not the same as previously reported. Since so little is known about the effect of drugs on the fetus, it is not inconceivable that there is an additive effect when drugs are used together. It is evident from Table IX that drugs are still very widely used by pregnant women, particularly during the first trimester. It may be reasonable to ask whether or not this use is excessive.

Complications and illness are not unusual during pregnancy. In the British Perinatal Mortality Survey[15] 6% of the mothers had bleeding during their pregnancy, 3.4% before 28 weeks. Sever and White[16] report that 5.3% of patients in 30,059 pregnancies had definite or presumed viral infections, not including the common cold. While the data in Table X might appear to suggest above-average infection or complication rates, in the absence of a control group it would be unwise to make such an assumption.

Conclusions

The preliminary investigation to date has provided no evidence to identify a specific etiologic agent. However, there is some geographic accumulation which suggests that an unusual number of infants with reduction deformities of the limbs were born in Alberta during the first six months of 1969. These findings justified the decision by the provincial authorities to undertake a more detailed follow-up of the cases in that province.

In the study reported in this paper there was insufficient evidence available to permit any decisions about etiology. In particular there are inadequate data about family histories, about the early growth and development of the mothers and their nutrition during the early months of pregnancy. There is almost no information about the amount of non-nutrients ingested during the first trimester and about the effect of other environmental influences not known to be teratogenic in man.

The results presented show that surveillance over the incidence of congenital anomalies is possible and can lead to a reasonably rapid follow-up of cases with specific anomalies. Further, the detection of such an episode would not have been possible without the existence of this pilot surveillance system. The proposed extension of this program to other provinces will likely increase its value. Such a follow-up may be required before full statistical proof of a significant trend is available. The information obtained using the follow-up tech-

TABLE X
Complications or illnesses during pregnancy reported for 29 mothers

Condition	*Trimester* 1st	2nd	3rd	unknown	*Total*
Nausea (severe)	5	1	1	—	7
Spotting or bleeding	3	—	—	—	3
Hydramnios	—	—	2	—	2
Toxemia	—	—	2	—	2
Urinary tract infection	2	1	1	1	5
Influenza	4	1	3	—	8
Pneumonia	1	—	—	—	1
Epileptic seizure	1	—	—	—	1
Total	16	3	9	1	29

TABLE XI
Selected congenital anomalies in infants born during first six months of each year reported to pilot study – surveillance system

Congenital anomaly	*1966* No.	Rate*	*1967* No.	Rate*	*1968* No.	Rate*	*1969* No.	Rate*
Anencephaly	37	77.9	35	74.4	44	94.9	35	72.3
Cleft lip alone	18	37.9	28	59.5	18	38.8	22	45.4
Cleft lip and/or cleft palate	75	158.0	72	153.1	75	161.7	64	132.1
Epispadias and hypospadias	42	88.5	50	106.3	51	110.0	54	111.5
Esophageal atresia and tracheo-esophageal fistula	8	16.8	11	23.4	3	6.5	6	12.4
Exomphalos and umbilical hernia	12	25.3	7	14.9	15	32.3	18	37.2
Imperforate anus	11	23.2	9	19.1	11	23.7	16	33.0
Polydactyly	48	101.1	29	61.6	37	79.8	28	57.8

*Per 100,000 live births.
See also Notes to Table I.

niques described in this paper is only adequate to rule out certain obvious teratogenic agents. It is quite insufficient to delineate genetic and exogenous factors.

The success of a program of surveillance must depend upon the realization by physicians that the accurate and complete reporting of all congenital malformations on vital statistics documents and on hospital records is essential and that this information is urgently required.

Résumé

Les malformations congénitales: rapport préliminaire d'une enquête sur les difformités atrophiques des membres. Le rôle d'un projet pilote de surveillance

Nous donnons ici un bref compte-rendu d'un projet pilote de surveillance des anomalies congénitales.

L'article expose les étapes nécessaires à franchir pour évaluer l'augmentation éventuelle du nombre de nouveau-nés qui présentent des difformités atrophiques des membres et donne les renseignements concernant 35 bébés nés dans quatre provinces au cours de 1969 et qui présentaient ces difformités.

On ne saurait assez souligner l'importance d'un maximum de précision dans les rapports des anomalies congénitales si on veut éviter de fausser les statistiques vitales et les dossiers hospitaliers.

Nous concluons comme suit: (1) le projet pilote de surveillance permet de mettre à jour les changements de fréquence des anomalies et de commencer l'étude ultérieure des cas dans un délai raisonnable; (2) les renseignements recueillis chez ces 35 malades ont été nettement insuffisants pour percer l'étiologie des anomalies: on n'a pas pu incriminer, dans la majorité des cas, de facteur étiologique connu et le besoin s'en fait sentir de plus en plus.

Members of the Biostatistics Division of the Research and Statistics Directorate, Department of National Health and Welfare, prepared data for evaluation and performed the statistical analyses. Dr. F. Clarke Fraser has been a constant source of advice and support during the investigation. Dr. James Miller and other members of the Expert Committee have given generously of their help. This study could not have been carried out without the unfailing co-operation of colleagues in New Brunswick, Manitoba, Alberta and British Columbia. Mrs. Yoneko Kawamoto, Division of Child and Maternal Health, prepared the tables and figures.

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Hereditary Angioneurotic Edema

In 1888 Sir William Osler firmly established hereditary angioneurotic edema as a familial entity, describing five generations of a family with gastrointestinal colic and swelling of the skin, with two deaths from laryngeal edema. However, the hereditary nature of this disorder may have been first described by Nathaniel Hawthorne in 1851. He told the story (The House of the Seven Gables) of a family with members who gurgled in the throat and chest when excited and who would sometimes die in this way, ever since a curse to choke on blood had been placed on one of their ancestors. That a hereditary disease, and not a curse, was responsible for their deaths is indicated by the following passage: "This mode of death has been an idiosyncrasy with this family, for generations past . . . Old Maule's prophesy was probably founded on a knowledge of this physical predisposition in the Pyncheon race."

The author describes a family with hereditary angioneurotic edema. Of 39 individuals, 11 are clinically affected in four generations, with two deaths from laryngeal edema; those still living have abnormally low levels of C'1 esterase inhibitor. Five children have the biochemical defect but as yet no symptoms. Four members of the family have symptoms suggestive of the disease but have normal sera; they may have other illnesses.

The most frequent precipitants of an attack are emotional stress and trauma. Minimal trauma to the extremities can cause swelling. Fatal laryngeal edema has followed dental extraction or tonsillectomy. Treatment of acute episodes is symptomatic. Various methods of prevention have been advocated but none are universally successful. Two of the males in the family described showed marked improvement when treated with sublingual testosterone.—J. J. Dennehy: *Ann. Intern. Med.*, 73: 55, 1970 (July).